

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, which comprises a compound of the formula (I)



in which

A is a monomer, multimer or polymer of TKPPR, or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B is a substrate[.] selected from the group consisting of B₁, a lipid able to bind the linker in a covalent or non-covalent manner and B₂, a non-lipid polymer able to bind the linker in a covalent manner.

Claims 2-3 (cancelled)

4. (original) A composition according to claim 1, wherein B comprises B₁, a lipid able to bind the linker in a covalent or non-covalent manner.

5. (original) A composition according to claim 4, in which B₁ comprises a synthetic or naturally occurring generally amphipathic and biocompatible compound, selected from the group consisting of fatty acids; lysolipids; phospholipids; phosphatidylinositol; sphingolipids; glycolipids; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids; lipids bearing polymers; lipids bearing sulfonated mono- di-, oligo- or polysaccharides; cholesterol, cholesterol

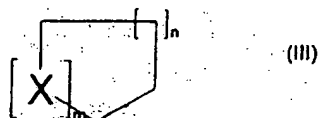
sulfate; cholesterol hemisuccinate; tocopherol hemisuccinate; lipids with ether and ester-linked fatty acids; polymerized lipids; diacetyl phosphate; dicetyl phosphate; stearylamine; cardiolipin; phospholipids with short chain fatty acids of about 6 to about 8 carbons in length; synthetic phospholipids with asymmetric acyl chains; ceramides; non-ionic liposomes; sterol esters of sugar acids; esters of sugars and aliphatic acids; saponins; glycerol dilaurate; glycerol trilaurate; glycerol dipalmitate; glycerol; glycerol esters; long chain alcohols; 6-(5-cholesten-3 β -yloxy)-1-thio- β -D-galactopyranoside; digalactosyl-diglyceride; 6-(5-cholesten-3 β -yloxy)hexyl-6-amino-6-deoxy-1-thio- β -D-manno-pyranoside; 12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoic acid; N-[12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)octadecanoyl]-2-aminopalmitic acid; N-succinyldioleoylphosphatidylethanolamine; 1,2-dioleoyl-sn-glycerol; 1,2-dipalmitoyl-sn-3-succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol; 1-hexadecyl-2-palmitoylglycerophosphoethanolamine; palmitoylhomocysteine, and combinations thereof.

6. (original) A composition according to claim 1, wherein B comprises B₂, a non-lipid polymer able to bind the linker in a covalent manner.
7. (original) A composition according to claim 6, in which B₂ comprises B_{2a} a polymer useful for producing microparticles, or B_{2b}, a non-ionic surfactant.
8. (original) A composition according to claim 7 in which B_{2a} is selected from the group consisting of polyvinyl alcohol (PVA) and a polyoxyethylene-polyoxypropylene block copolymer.
9. (original) A composition according to claim 7, in which B_{2a} comprises a bead which is derivatizable and is attached to a detectable label.

Claims 10-22 (cancelled)

23. (original) A composition according to claim 1, in which L is a bond or is derived from: an alkyl chain $C_1.C_{6000}$, linear or branched, saturated or unsaturated, optionally interrupted or substituted by one or more groups such as: O, S, NR, OR, SR, COR, COOH, COOR, CONHR, CSNHR, C=O, S=O, S(=O)₂, P=O(O)₂OR, P(O)₂(OR)₂, halogens, or phenyl groups, optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens, in which R is H or an alkyl group C_1-C_4 , linear or branched, optionally substituted by one or more — OH; such a chain can be interrupted or substituted by one or more cyclic groups $C_3.C_9$, saturated or unsaturated, optionally interrupted by one or more O, S or NR; by one or more groups such as: -NHR, -OR, -SR, -COR, -CONHR, or a phenyl group optionally substituted by one or more -NHR, -OR, -SR, -COR, -CONHR, -N-C=S, -N-C=O, halogens.

24. (original) A composition according to claim 23, in which the cyclic groups present in L are saturated or unsaturated, and correspond to the following general formula (III)



in which

n can range from 0 to 4;

m can range from 0 to 2;

X can be NH, NR, O, S or SR.

25. (original) A composition according to claim 23, in which the linker L is an oligopeptide comprising 1 to 100 natural or synthetic amino acids.

26. (original) A composition according to claim 25, in which the amino acids are selected from the group consisting of glycine, glutamic acid, aspartic acid, γ -amino-butyric acid and trans-4-aminomethyl-cyclohexane carboxylic acid.
27. (original) A composition according to claim 23, in which L is derived from difunctional PEG(polyethyleneglycol) derivatives.
28. (original) A composition according to claim 23, in which L is selected from the group consisting of: glutaric acid, succinic acid, malonic acid, oxalic acid and PEG derivatized with two CH_2CO groups.
29. (original) A compound of the formula (IIa) for use in targeting endothelial cells, tumor cells or other cells which express NP-1

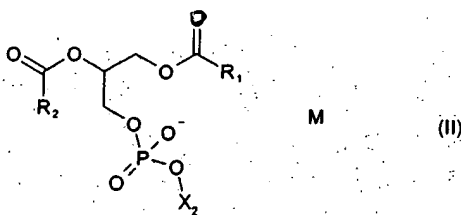


in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

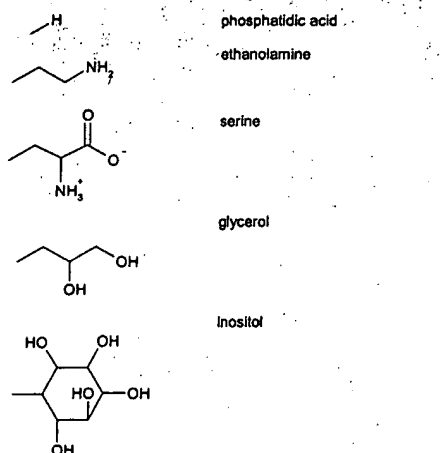
B_{1a} comprises a phospholipid moiety of the formula (II),



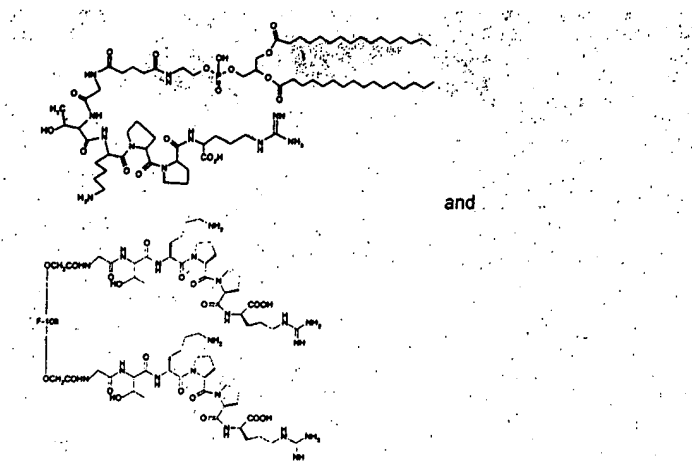
where

M is an alkaline or alkaline- earth metal cation;

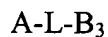
R_1 and R_2 independently, correspond to a linear long chain C_{12} - C_{20} ; saturated or unsaturated, optionally interrupted by $C=O$, or O ; and X_2 is selected in a group consisting of



30. (original) A compound according to claim 29, in which R_1 and R_2 are independently a saturated linear long chain C_{12} - C_{20} .
31. (original) A compound according to claim 30, in which the phospholipid of formula (II) comprises a phospholipid selected from the group consisting of:
dimyristoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine,
distearoylphosphatidylethanolamine, diarachidoylphosphatidylethanolamine,
dioleylphosphatidylethanolamine, dilinoleylphosphatidylethanolamine, fluorinated analogues of
any of the foregoing, and mixtures of any of the foregoing.
32. (original) A compound according to claim 31, in which the phospholipid of formula (II) comprises dipalmitoylphosphatidylethanolamine.
33. (original) A composition for use in targeting endothelial cells, tumor cells or other cells which express NP-1, comprising a compound selected from the group consisting of:



34. (original) An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of any one of claims 29 to 32.
35. (original) An ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of claim 29 and the gas comprises a fluorinated gas.
36. (original) An ultrasound contrast agent comprising a suspension of gas-filled microbubbles in which the microbubbles comprise a compound of claim 29 in which A is TKPPR tetramer and the gas comprises SF₆, or a perfluorocarbon selected from the group consisting of C₃F₈, C₄F₈, C₄F₁₀, C₅F₁₂, C₆F₁₂, C₇F₁₄ and C₈F₁₈.
37. (original) A compound for use in targeting endothelial cells, tumor cells or other cells that express NP-1 of the formula



where

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells that express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B₃ is a biodegradable, physiologically acceptable polymer.

38. (original) An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37.

39. (original) An ultrasound contrast agent comprising a suspension of gas-filled microballoons, in which the microballoons comprise a compound of claim 37 in which A is a TKPPR tetramer and the gas comprises a gas selected from the group consisting of: air; nitrogen; oxygen; CO₂; argon; xenon or krypton, a fluorinated gas, a low molecular weight hydrocarbon, an alkene or an alkyne and mixtures thereof.

Claims 40-48 (cancelled)

49. (original) A method of ultrasound imaging comprising administering an ultrasound contrast agent comprising a suspension of gas-filled microbubbles, in which the microbubbles comprise a compound of the formula (IIa)

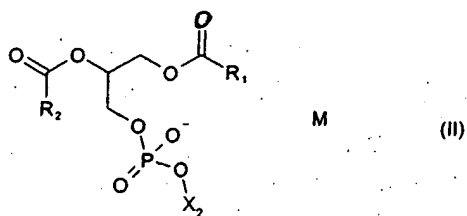


in which

A is a monomer, multimer or polymer of TKPPR or a TKPPR analogue which specifically binds to NP-1 or cells which express NP-1 with avidity that is equal to or greater than TKPPR;

L is a linker; and

B_{1a} comprises a phospholipid moiety of the formula (II),

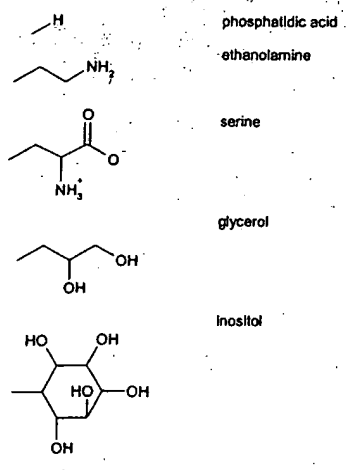


where

M is an alkaline or alkaline- earth metal cation;

R₁ and R₂ independently, correspond to a linear long chain C₁₂-C₂₀; saturated or unsaturated, optionally interrupted by C=O, or O; and

X₂ is selected in a group consisting of



Claims 50-65 (cancelled)